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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/580,511	02/13/2007	Elaine Fuchs	RCK0017US.NP	2375
26259 7590 06/15/2010 LICATA & TYRRELL P.C. 66 E. MAIN STREET MARLTON, NJ 08053				
EXAMINER TON, THAIAN N				
ART UNIT 1632		PAPER NUMBER		
NOTIFICATION DATE 06/15/2010		DELIVERY MODE ELECTRONIC		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

porcilly@licataandtyrrell.com

**Advisory Action**  
**Before the Filing of an Appeal Brief**

**Application No.**

10/580,511

**Applicant(s)**

FUCHS ET AL.

**Examiner**

Thaia N. Ton

**Art Unit**

1632

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 02 June 2010 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.  
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.  
Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**NOTICE OF APPEAL**

2. ☐ The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

**AMENDMENTS**

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);  
(b) ☐ They raise the issue of new matter (see NOTE below);  
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.  
NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.

6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: 1.

Claim(s) objected to: \_\_\_\_\_.

Claim(s) rejected: 7 and 8.

Claim(s) withdrawn from consideration: \_\_\_\_\_.

**AFFIDAVIT OR OTHER EVIDENCE**

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

**REQUEST FOR RECONSIDERATION/OTHER**

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.

12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). \_\_\_\_\_

13. ☐ Other: \_\_\_\_\_.

/Thaia N. Ton/  
Primary Examiner, Art Unit 1632

Continuation of 5. Applicant's reply has overcome the following rejection(s):

1. The rejection of claims 2-5 under 35 U.S.C. 102(b) as being anticipated by US Pat No. 5,665,557 (Filed November, 1994; Issued September 9, 1997) as evidenced by Schrieber et al (Haematologica, 94(11): 1493-1501, 2009) and further evidenced by Akashi et al. (Blood, 101(2): 383-390, 2003). This rejection is withdrawn in view of Applicants' cancellation of the claims.
2. The rejection of claims 2-5, 7-16 under 35 U.S.C. 102(a) as being anticipated by Tumber et al. (Science, 303: 359-363, January 2004, available online December 11, 2003). This rejection is withdrawn in view of Applicants' filing of a 1.132 Declaration by Elaine Fuchs, Tudorita Tumber, Cedrick Blanpain and William E. Lowry.
3. The rejection of claims 1-5 under 35 U.S.C. 103(a) as being unpatentable over Tumber et al. (Science, 303: 359-363, January 2004, available online December 11, 2003 when taken with US Pat No. 5,665,557 (Filed November, 1994; Issued September 9, 1997). This rejection is withdrawn in view of Applicants' filing of a 1.132 Declaration by Elaine Fuchs, Tudorita Tumber, Cedrick Blanpain and William E. Lowry.

Continuation of 11. does NOT place the application in condition for allowance because:

Claims 7 and 9 stand rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat. No. 5,639,618 (Filed May 13, 1994, Issued June 17, 1997, IDS) when taken with Strathdee et al. (Gene, 229: 21-29, 1999), Bohl et al. (Nat. Med., 3(3): 229-305, 1997) when taken with Mahmud et al. (Blood, 97(10): 3061-3068, 2001) and US Pat. No. 6,485,971 (filed September 18, 2000, Issued November 26, 2002). Applicants argue that the rejections of record do not identify how every limitation of the claimed invention is found in the references (p. 9 of the Response). In particular, Applicants argue that the rejection does not identify where in the references the active steps of instant claim 7 d)-g) are found, and a mere teaching of the use of antibodies, FACS techniques, sorting of slow-cycling cells from rapidly dividing cells does not constitute a teaching or suggestion of steps d)-g). Applicants argue that the Office action does not support a conclusion of obviousness. Applicants argue that the prior Office actions' assertion that one of skill in the art would arrive at the claimed invention provides no factual basis or evidence to support the Examiner's conclusion, and that at most, the express disclosure of Mahmud's fairly reads as teaching that subpopulations of bone marrow cells can be isolated by Hoechst/Rodamine staining and CD34+ selection, and that BrdU content of different subsets of cells is indicative of the replicative history of the cells. Likewise, Applicants assert that the '971 document fairly reads on methods of enriching for a viable subpopulation of epidermal cells having an altered proliferative potential compared with an unfractured population of epidermal cells based upon a higher level of cell surface integrin expression and expression of transferrin receptor< EGFR, IGFR or keratinocyte growth factor receptor. As such, the teachings of the references themselves lead the skilled artisan to conclude that surface markers and dye exclusion can be used to sort cells, but there is simply no nexus to bridge the gap between the teachings of these references. See page 10 of the Response.

These arguments have been considered but not persuasive. In the instant case, the Examiner contends that the combination of art as a whole is sufficient to arrive at the claimed invention. In particular, the guidance for using a reporter protein in cell sorting to isolate a specific type of stem cell is found in the '618 document. Strathdee and Bohl provide guidance to show that the Tet system would be useful in regulating gene expression in stem cells. Thus, addition of a reporter gene, such as GFP, which is taught in the '618 document, would be fully recognized by the skilled artisan as a method to monitor cell-specific expression in order to separate the cells using the cell sorting methods taught by the '618 document. Thus, it would be obvious that the vectors taught by Strathdee and Bohl could be modified to incorporate a reporter gene for use in the sorting methods taught by the '618 patent.

Mahmud provide guidance to show that the skilled artisan would recognize that stem cells are considered slow-cycling cells, and that the enriching steps, such as those taught in the '971 document are also known in the art (col. 3, lines 49-col. 4, lines 1-12, for example). Thus, Mahmud teach that stem cells are slow-cycling, which would clearly maintain higher levels of reporter protein than cells that are dividing, and the '971 document provides clear guidance as to how to separate cells that have higher versus lower levels of protein expression. One of skill in the art would be further motivated, in view of the teachings of Mahmud and the '971 document, to inactivate the regulatable transcription factor (by, for example, the withdrawal of doxycycline in the case of using the Tet system), and select for slow-cycling stem cells by allowing the cells to divide, and selecting cells that contain a higher level of reporter protein expression. The fact that stem cells are slow-cycling cells, withdrawal of doxycycline, and then allowing the slow-cycling cells to divide would provide a distinction in concentration of reporter gene when compared to non-slow cycling cells. The Examiner contends that each step of the claimed invention is obvious over the cited art of record and the rejection is maintained.

Claim 8 stands rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat. No. 5,639,618 (Filed May 13, 1994, Issued June 17, 1997, IDS) when taken with Strathdee et al. (Gene, 229: 21-29, 1999), Bohl et al. (Nat. Med., 3(3): 229-305, 1997) when taken with Mahmud et al. (Blood, 97(10): 3061-3068, 2001) and US Pat. No. 6,485,971 (filed September 18, 2000, Issued November 26, 2002) as applied to claims 7 and 9 above, and further in view of US Pat No. 5,665,557 (Filed November, 1994; Issued September 9, 1997). Applicants provide the same arguments as above, which have been addressed.